REMARKS/ARGUMENTS

The final Office Action mailed January 14, 2004, has been received and reviewed. Applicants also acknowledge and express appreciation to the examiner for permitting a telephone interview, during which the outstanding issues were discussed, and the Examiner recommended that the Applicant's file a response to the office action, together with the above-proposed amendments, in connection with an RCE.

Claims 13-36 are currently pending in the application. Claims 13-26 stand rejected. Applicants have amended claims 13 so as to place all claims in condition for allowance (all of claims 14-26 are dependant on claim 13), and respectfully request reconsideration of the application as amended herein.

Claim Amendment

As noted in the previous section, claim 13 has been amended to clarify the claimed subject matter. Specifically, Applicant has replaced the term "tube" with the term "reaction vessel," and has also indicated that the reaction vessel is "containing a mixture" of the reagents, making it clear that the sequencing reagents are mixed together in a single reaction vessel, and not merely placed in the same container or box in separate vessels. The current terminology is thus incompatible with the Examiner's previous construction, which broadly defined "tube" as encompassing containers and boxes. Support for the term "reaction vessel" is found, for example, in the Specification at page 3, line 24 ("single reaction vessel"). Support for the terms "mixture" is found, for example, in the Specification at page 3, line 19 ("single reaction mixture"), page 4, line 19-20 ("mixture of four deoxynucleotide triphosphates and at least one dideoxynucleotide triphosphate"), and page 12, line 25 ("kit will suitably include at least one pre-prepared mixture comprising all four nucleotide triphosphates and at least one chain terminating nucleotide triphosphate"). The amendments are therefore supported by the Specification.

Applicant has also amended the claim to clarify that the region-specific reagents are "sequencing" reagents, and that such reagents "comprise region-specific primers, deoxynucleotide triphosphate feedstocks, at least one chain terminating dideoxynucleotide triphosphate and a thermally stable polymerase enzyme capable of incorporating

dideoxynucleotides into an extending nucleic acid polymer." These amendments further clarify the claimed subject matter. Support for the recited reaction reagents is found, for example, in the Specification at page 4, lines 1-4 ("wherein said region-specific sequencing reagents comprise region-specific primers, deoxynucleotide triphosphate feedstocks, at least one chain terminating dideoxynucleotide triphosphate and a thermally stable polymerase enzyme capable of incorporating dideoxynucleotides into an extending nucleic acid polymer"). The amendments are therefore supported by the Specification.

Summary of Claimed Invention

The present invention is directed to a kit for sequencing one or more DNA regions from a sample, consisting of, in packaged combination, a reaction vessel containing a mixture of region-specific sequencing reagents sufficient for each DNA region to be sequenced and optionally in said mixture one or more non-region specific sequencing reagents, wherein said region-specific sequencing reagents comprise region-specific primers, deoxynucleotide triphosphate feedstocks, at least one chain terminating dideoxynucleotide triphosphate and a thermally stable polymerase enzyme capable of incorporating dideoxynucleotides into an extending nucleic acid polymer.

The kits of the present invention comprise reagents in a single tube to form a reaction mixture of primers combined with the reagents. The method of using the kit of the present invention is the subject of granted U.S. Patent No. 6,214,555.

Claim Rejections Under 35 USC §102

The Examiner has rejected claims 13-16, and 25-28 under 35 U.S.C. §102(e), as being anticipated by Jordan et al. (U.S. Patent No. 6,017,699, filed March 29, 1996). The Examiner specifically states that Jordan et al. teaches "a kit consisting of, in package combination, region-specific reagents for a genomic DNA sample of a microorganism (col. 6, lines 55 to col. 7, line 4), wherein the region-specific reagents comprises a pair of primers which binds to the sense (coding) and antisense (noncoding) strands (col. 10, lines 7-17)" and concludes that "[t]herefore, Jordan meets the limitations of claims 13-16 and 25,28." The Examiner's rejection is based on the interpretation that the term "tube," as previously used in claim 13, can be interpreted broadly enough to encompass a box or container in which the contents of the kit are packaged.

Applicants have amended the claims to clarify that the claims cover region-specific sequencing reaction reagents are in a "mixture" in a "single reaction vessel," thus precluding the construction suggested by the examiner. The limitation that the region-specific sequencing reaction reagents are in a "mixture" requires that the reagents be physically combined within a single reaction vessel, precluding a construction that they be present in the same box where they would not be mixed. Similarly, the claims require that the mixture of region-specific sequencing reaction reagents be present in a "single reaction vessel," which further clarifies that the mixture be present in only a single vessel in which the reaction takes place, precluding an interpretation that the reagents could be in different vessels in the same container (the reaction could not take place if the reagents were not mixed in a single reaction vessel.) The claims also require that the region-specific sequencing reagents be "sufficient for each DNA region to be sequenced" and include "region-specific primers, deoxynucleotide triphosphate feedstocks, at least one chain terminating dideoxynucleotide triphosphate and a thermally stable polymerase enzyme capable of incorporating dideoxynucleotides into an extending nucleic acid polymer."

Jordan does not therefore establish the limitations of the claims. Specifically, Jordan does not disclose a "single reaction vessel." Although Jordan discloses packaging of various reagents in a "kit packaged combination," there is no teaching or suggestion that the sequencing reaction reagents be in a "mixture" or that the mixture is present in a "single reaction vessel," as required by the claims. The Examiner's suggestion that Jordan's reference to a "kit in packaged combination" implies that "the reagents of the kit are packaged together in a single tube" is untenable. Jordan teaches that the reagents are "in a *kit* packaged combination," that the "*kit* can comprise in packaged combination with other reagents," that the "*kit* can further include in the packaged combination buffers," and that the "*kit* may optionally contain a denaturation solution." None of the above references to the contents of the kit in any way imply that the reagents in the kit are in a "mixture" or that they are in a "single reaction vessel," since the contents of a kit may be (and normally would be) in separate tubes of reagents combined in a single shipping container. Furthermore, the Examiner's position that a "single tube of region-specific reagents ... can broadly be interpreted as the region-specific reagents each being in a separate container or tube" is untenable, since the terms "single" and "separate" have opposite meanings and are mutually inconsistent. Even the most fundamental rules of claim construction do not permit one to arbitrarily construe a term so as to encompass its opposite meaning. Notwithstanding the

fallacy of the Examiner's position, the Applicant has amended the claims to clarify that the sequencing reagents are in a "mixture" and in a "single reaction vessel" (not merely in the same shipping container or box), which clearly indicates that the reagents are physically mixed, and not in separate tubes within the same package. Accordingly, Applicant respectfully requests that the above rejection be withdrawn.

The Examiner has also rejected claims 13, 14, 16, 25-26, and 28 under 35 U.S.C. §102(e), as being anticipated by Vasta et al. (U.S. Patent No. 6,326,485, effective filing date of July 26, 1996). Vasta discloses a kit for amplifying DNA which "comprises a container having a pair of outwardly-directed PCR primers to the NTS region of the microorganism(s) being tested for." The Examiner rejects the claims on grounds that Vasta et al. teach the use of a pair of primers for PCR amplification reactions, which is argued anticipates the claim language reciting "region-specific reagents." This rejection also appears to be based on the claim construction that the term "tube," as previously used in claim 13, can be interpreted broadly enough to encompass a box or container in which the contents of the kit are packaged.

For the same reasons discussed above in connection with Jordan, Applicants' amended claims clarify that the region-specific sequencing reaction reagents are in a "mixture" in a "single reaction vessel," thus precluding the illogical construction suggested by the Examiner that a "single tube . . . can be broadly interpreted as . . . separate container or tube." Moreover, the teaching of Vasta et al. of a kit for amplifying DNA which "comprises a container having a pair of outwardly-directed PCR primers to the NTS region of the microorganism(s) being tested for" is at best ambiguous with respect to whether the primers are located in a single reaction vessel. Even if Vasta et al. were interpreted as including the primers in the same reaction vessel, it is clear that the other reagents are not present in the same container. By stating that the "*kit* preferably comprises *a container* having a pair of outwardly-directed PCR primers" and that "[t]he *kit* would *also* include the buffers, DNA polymerase, and dideoxynucleotides, KCl_2 and $MgCl_2$ and all other reagents necessary to conduct PCR amplification," Vasta et al. imply that the other reagents, while in the kit, are not within the container. In contrast, Applicants' claims, which now require that the region-specific sequencing reagents are in "mixture" in a "single reaction vessel," which distinguishes over the cited prior art.

Claim Rejections Under 35 USC §103

The Examiner has also rejected claims 17-24 and 29-36 as being unpatentable over Ruano (U.S. Patent No. 5,427,911), in view of Rao (Analytical Biochemistry, Vol. 216, pages 1-14, 1994) and further in view of Ahern (The Scientist, Vol. 9, No. 14, pages 1-15, June 1995).

Rao et al. disclose the method of generating DNA sequence from PCR-amplified DNA using two locus specific primers. The present invention is distinguishable over the method disclosed by Rao et al., which uses radiolabeled primers, all labeled with the same isotope. Because the radiolabeled primers are all labeled with the same isotope, they necessarily must be kept in separate tubes, otherwise the labeled products could not be distinguished from each other. The method of Rao et al. is therefore inconsistent with, and cannot therefore teach or suggest, the kits of the present invention, which require that the reagents be mixed in the same reaction vessel.

Similarly, Ruano et al. do not teach or suggest the limitations of the present invention, which require that the reagents be mixed in a single tube. The Examiner states that Ruano et al. teaches that the reagents may be in a single container, quoting the following passage from Ruano: "The present invention encompasses kits for conducting the aforementioned processes. Such kits include in one or more containers, a set of instructions, and one or more of a thermally stable enzyme." In this passage, the reference to the term "containers," which includes "a set of instructions" clearly refers to packaging containers (such as a box), not the reaction vessel, since the reaction vessel would obviously not contain "a set of instructions." Furthermore, as is evident from Figure 5 in Ruano et al., the labeled primers are placed into separate tubes 12. Ruano et al. also does not suggest the present invention, which requires that the reagents be mixed in the same reaction vessel.

Ahern et al. only disclose that kits may be desirable, and does not disclose any specific details of the arrangement or contents of a kit.

Moreover, the combination of the above prior art references do not suggest the claimed invention. Significantly, the Examiner's rejections are all predicated on an interpretation of the previous claim language that the term "container" includes the packaging (i.e., the box in which the kit is assembled or shipped). The amendments to the claims now make it clear that the reagents are mixed in a single reaction vessel. None of the above three references (Rao, Ruano

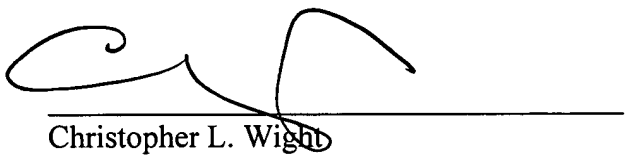
or Ahern), either alone or in any combination, disclose reagents that are mixed in a single reaction vessel. Accordingly, the rejection cannot be maintained and should be withdrawn.

CONCLUSION

The Examiner's previous rejections appear to have been predicated solely on an interpretation of the claims that is inconsistent with the meaning and intent of the Applicant, and the language of the specification. Applicants have amended the claims in such a manner as to preclude the Examiner's interpretation, and clarify that the reagents are mixed in a single reaction vessel. In view of this amendment, Applicant believes that the claims cannot now be interpreted as suggested by the Examiner, and that the claimed kits are not therefore taught or suggested by the cited references.

For the above reasons, Applicants respectfully request that the claims of the application be allowed and proceed to issuance.

Respectfully submitted,



Christopher L. Wight
Registration No. 31,680
Holland & Hart LLP
555 17th Street, Suite 3200
Denver, CO 80201-8749
Telephone: (801) 595-7823
Fax: (303) 295-8261

CLW/jml
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Examiner's Rejection	Response
Jordan (US 6,017,699) "kit consisting of, in packed combination, region-specific reagents for a genomic DNA sample of a microorganism" (col. 6, line 55 to col. 7, line 4) "single tube of region-specific reagents ... can broadly be interpreted as the region-specific reagents each being in a separate container or tube" (emphasis added) "specification does not specifically define the kit as having all the region specific reagents in a single tube" "packed in combination...thus implying that the reagents of the kit are packaged together in a single tube"	Jordan teaches "kit preferably *comprises* a container having a pair of outwardly-directed PCR primers to the NTS region of the microorganism(s) being tested for." (col. 12, line 54 to col. 13 line 4). Not equivalent to kit "consisting" of single tube.... Kit of Jordan discloses amplification primers, not sequencing primers. Claim to "single tube" is explicit "containing a mixture" further clarifies relationship of region-specific reagents "Packaged in combination" does not imply "packaged together in a single tube" imply = suggest as a logically necessary consequence
Vasta (US 6,326,485) Vasta discloses a kit consisting of, in a single container a region-specific reagent for a DNA region, wherein the region-specific reagents comprise a pair of primers which binds to the sense and antisense strands and flank the region of microorganism DNA "single tube . . . can be broadly interpreted as . . . separate container or tube" "The specific primers described here can be incorporated into a kit for detection of P. marinus at various stages of oyster development. The rapid amplification of large numbers of samples may be analyzed to	Vasta does not disclose single container Vasta teaches "kit comprises a container having a pair of outwardly directed PCR primers..." **NO REFERENCE TO "SINGLE" CONTAINER!**

Examiner's Rejection	**Response**
determine variation in population densities in environmental samples or to assay infection intensities from a large group of experimentally infected oysters. This kit preferably comprises a container having a pair of outwardly-directed **PCR primers** to the NTS region of the microorganism(s) being tested for. This kit can have any of the PCR primers listed in FIG. 5 or a combination thereof. One skilled in the art will readily recognize that the number and type of primers which are in the kit will depend on the use of the kit as well as the sequences to be detected. The kit would also include the buffers, DNA polymerase, and dideoxynucleotides, KCl_2 and $MgCl_2$ and all other reagents necessary to conduct PCR amplification." (Vasta, col. x, lines x-x)	
Ruano (US 5,427,911) Ruano shows "one [single] or more containers" ddNTPs in mole ratio of 1:10	The present invention also encompasses kits for conducting the aforementioned processes. Such kits include in one or more containers, a set of instructions, and one or more of a thermally stable enzyme, e.g., Taq polymerase, salts, e.g., KCl and $MgCl_2$, Tris, deoxynucleotides... and labeled primers." (col 8, lines 4-12) Because specification states that kit includes in one or more containers "a set of instructions", it is obvious that the "container" means box for the kit, not a "reaction vessel", since instructions would not be placed in a reaction vessel. Also, Figure 5 explicitly shows use of separate reaction vessels for labeled primers for A and B regions. Specification also clearly states that "[t]he amplified material (template) from tube 10 is split into two aliquots 12." (col. 6, ll. 34-35)

Examiner's Rejection	**Response**
Rao (Anal. Biochem) direct sequencing of PCR amplified DNA sequencing genomic DNA by amplifying locus specific primers flanking target region, synthesizing truncated strands by introducing dideoxynucleotide terminators and labeled terminator "Rao teaches ... region specific reagents are placed in a separate single tube" [radio labeled primers, all with same label]	Rao uses radiolabeled primers, labeled with same isotope, which necessarily requires that they be placed in separate reaction vessels since they cannot be distinguished in a single reaction vessel. "separate single" is oxymoronic, inherently contradictory
Ahern (Scientist) kit	throw-away citation for "kit"